UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,542	01/18/2002	Christoph Gebhardt	113737.7	6594

23973 7590 11/28/2005

DRINKER BIDDLE & REATH
ATTN: INTELLECTUAL PROPERTY GROUP
ONE LOGAN SQUARE
18TH AND CHERRY STREETS
PHILADELPHIA, PA 19103-6996

EXAMINER	
JOHNSTON, PHILLIP A	
ART UNIT	**PAPER NUMBER**
2881	

DATE MAILED: 11/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

EJ C

Office Action Summary	Application No.	Applicant(s)
	10/031,542	GEBHARDT ET AL.
	Examiner	Art Unit
	Phillip A. Johnston	2881

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

Detailed Action

1. This Office Action is submitted in response to amendment dated 9-13-2005, wherein claims 1-21 were previously canceled. Claims 22-52 are pending.

Claims Rejection – 35 U.S.C. 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

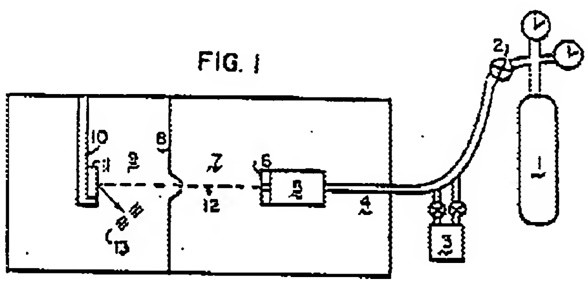
3. Claims 22-29,31,34-40,42,43,45,46,48,49,51, and 52 stand rejected as being unpatentable over U.S. Patent No. 4,845,367 to Amirav, in view of Friedman, U.S. Patent No. 4,755,344.

Amirav (367) discloses the following;

(a) In Figure 1, an apparatus and method for producing ions by impinging a molecular beam 12 onto a solid surface 11, wherein a light gas (hydrogen or helium), or gas mixture, is supplied from a container 1 via a gas valve 2, which may be manually or remotely controlled to initiate the ion source. The substance to be ionized is supplied from a container 3. The gas from container 1, is first seeded (gas phase loading) with the substance to be ionized through 4 to a heating element 5 and then through a supersonic nozzle 6 disposed within a vacuum chamber 7.

Supersonic nozzle 6, which may have continuous or pulsed operation (as recited in claim 34), produces a hyperthermal beam of the gas of container 1 seeded with the substance of container 3 to be ionized. The supersonic beam 12 , is directed through a skimmer and skimmer holder 8 into a high or ultra-high vacuum chamber and impinged on a solid surface 11 to induce molecular ionization or dissociative ionization. The ions so produced are extracted by an ion extractor 13, into a quadrupole mass analyzer where fragmentation spectra are obtained, as recited in claims 22-26,28,29,34,36,37 40,43, 46,49 and 52. See Column 3, line 30-42; and Figures 1 and 2 below;

FIG. 1



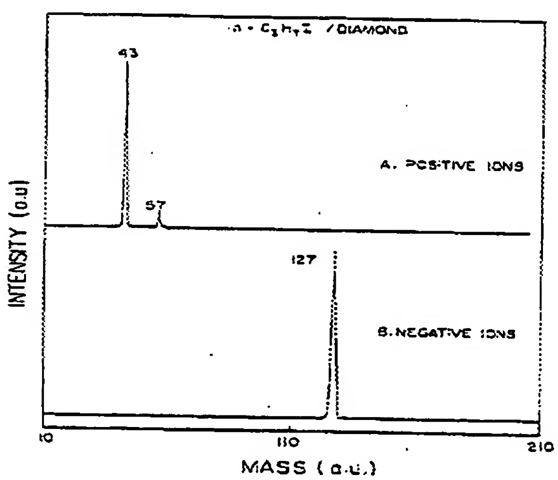


FIG 2

(b) Impinging clusters on solid surfaces to initiate reactions, as recited in claims 24-26,28,31,39,45, and 48. See Column 1, line 48-58; and Column 2, line 43-65;

(c) Fragmenting chemically converted samples through excitation and forming both positive and negatively charged fragments, as recited in claims 22, 26, and 36. See Column 2, line 55-68; and Figure 3 below;

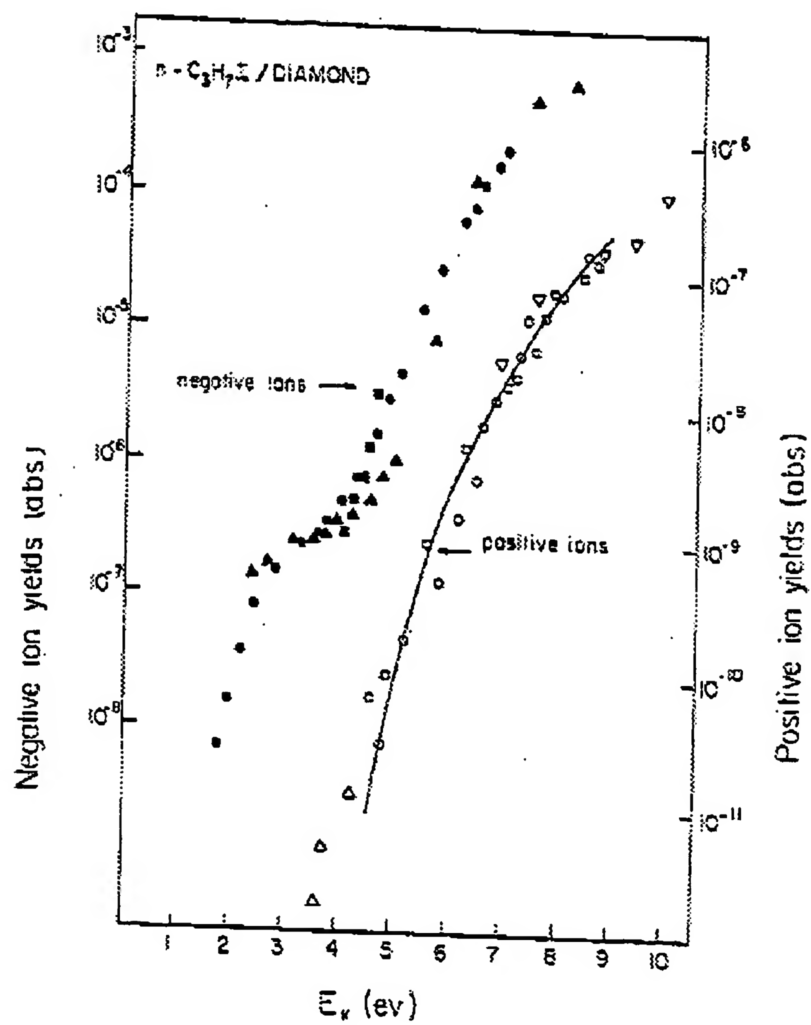


FIG 3

(d) Utilizing an angle of impingement of 22.5 degrees, as recited in claim 38. See Column 4, line 21-45.

(e) The use of single crystal diamond or molybdenum for the solid surface 11, as recited in claims 40,43, and 49.

Amirav (367) as applied above fails to teach producing neutral clusters composed of polar molecules, as recited in claims 22 and 27. However, Friedman (344) discloses that it is known in the art to form neutral clusters of water containing up to 28 water molecules by the supersonic expansion of a gas through a nozzle, as recited in claims 22 and 27. See Column 1, line 48-63; and Column 2, line 27-41.

Therefore it would have been obvious to one of ordinary skill in the art that the cluster fragmentation method of Amirav (367) can be modified to use the carrier gas containing water molecules in accordance with Friedman (344), to provide a method for the generation of large cluster ions formed by expansion of gases through a supersonic nozzle.

4. Claims 30,32,33,41,44,47, and 50 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Amirav (367) and Friedman (344) in view of Aberth (669), U.S. Patent No. 4,851,669.

The combination of Amirav (367) and Friedman (344) discloses nearly all the limitations of claims 30,32,33,41,44,47, and 50, but fail to teach the use of (a) an alkali reaction partner, as recited in claim 30; (b) reactive surfaces coated with an acid or base material, as recited in claims 32, and 33; and (c) reaction partner coatings with a surface density whose temporal average has a predetermined value, as recited in

claims 41,44,47, and 50. However, Aberth (669) disloses that it is known to direct neutral clusters at a target, where the resultant ions are mass analyzed, and further discloses the use of ion source 12 to impinge Cesium cluster ions upon a sample coated collision target plate 16, and producing fragmentation shown in Figure 10 below, as recited in claims 30,32, and 33. See Column 4, line 20-60; Column 8, line 45-65; and Figure 10 below.

It is implied herein that the coating surface density of Aberth (669) has a predetermined temporal average, as recited in claims 41,44,47, and 50.

Therefore it would have been obvious to one of ordinary skill in the art that the cluster fragmentation apparatus and method of Amirav (367) and Friedman (344) can be modified to use the resitive element forming method of Aberth (669), to provide collisional dissociation of parent ions in tandem mass spectrometric analysis of a material sample, thereby allowing application to a broad range of compounds, including relatively high molecular weight biological compounds.

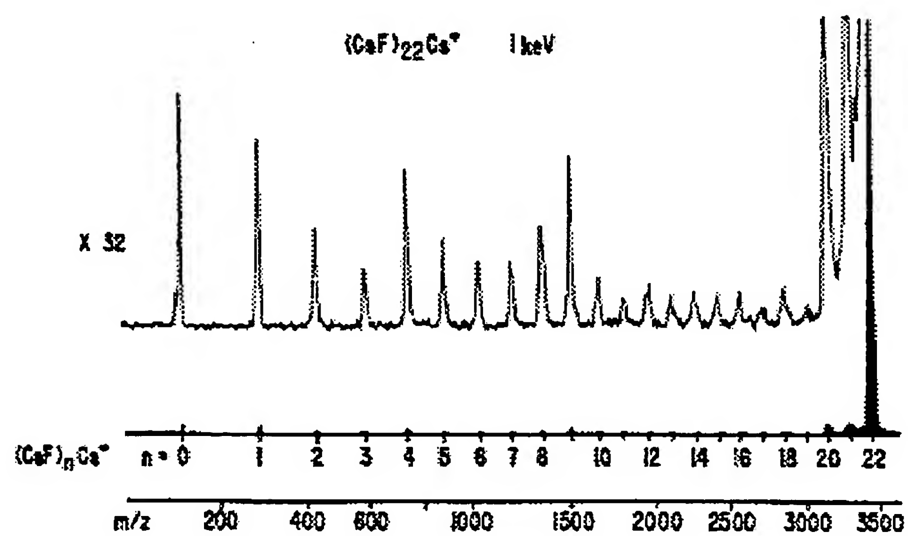


FIG._10.

Examiners Response to Arguments

5. Applicant's arguments filed 9-13-2005 have been fully considered but they are not persuasive.

Arguments 1 and 2.

Applicant states that "Nowhere does Amirav discuss forming a neutral cluster of polar molecules and loading the neutral cluster with a reaction partner, where the reaction partner is chemically different from the molecules of the neutral cluster. Further, Applicants respectfully submit that as a result, Amirav cannot teach the formation of at least one pair of differently charged charge carriers by a carrier substance and reaction partner. Finally, Applicants respectfully submit that Amirav does not teach cluster fagmentation as recited in Claim 22, but rather molecular fragmentation.

As a result, Applicants respectfully submit that Amirav does not teach each and every element of Claim 22."

Applicant also states that " In the first instance, as stated above, Amirav does not teach cluster formation or fragmentation at all. Further, Friedman is drawn to the formation of cluster ions, not neutral clusters. Friedman, col. 1, lns. 23-27. The reference to a cluster containing up to 28 water molecules also states that the cluster contains a single proton. Friedman, col. 2, lns. 29-36.The cluster ions of Friedman are formed by ionizing a gas by means of an electrode, then expanding the gas containing

ions and electrons through a supersonic nozzle into a region of low pressure. Friedman, col. 3, lns. 23-32. Therefore, Applicants respectfully submit that even if one were to combine Amirav and Friedman the combination would not cure the fundamental deficiency of Amirav recognized by the Examiner. Additionally, neither Amirav nor Friedman teach the formation of at least one pair of differently charged charge carriers by interaction of a reaction partner and a carrier substance in a neutral cluster as recited in Claim 22. In Amirav a charge is produced by impinging a substance to be ionized against a solid surface to either add or subtract an electron, or induce molecular dissociation. Friedman utilizes an electrode to induce ionization prior to cluster formation. Further, neither Amirav nor Friedman teach cluster fragmentation to produce oppositely charged cluster fragments as recited in Claim 22. Friedman does not teach fragmentation at all, and Amirav teaches molecular fragmentation.

Applicants therefore respectfully submit that the combination of Amirav and Friedman does not disclose each and every element of Claim 22."

Regarding disclosure of the use of <u>polar molecules in carrier substances and formation of at least one pair of differently charged charge carriers by a carrier substance and reaction partner</u> by Amirav (367);

The applicant is respectfully directed to page 7 of applicant's specification, which states; The carrier substance, through which the clusters are formed, is preferably made of polar molecules, i.e. of molecules which have their own dipole moment, for example HaO, SO2, NO2, NH3, NOa, SFn, CH3CN, CHClFZ, or isobutene.

The applicant is also respectfully directed to Amirav (367), Column 2, line 10-20, which states; Theoretically, almost any molecule or atom can be used for producing positive ions, and almost any molecule, atom, or molecule with a fragment having a high electron affinity can be used for producing negative ions. Halides generally have high electron affinity and therefore are particularly useful for producing negative ions: examples which have been found operative are the alkyl halides, such as propyl iodide, ethyl iodide, and butyl iodide, and hexafluorobenzene. For producing positive ions, there may be used anthracene benzylbromide, and $C_4 H_4 N_2$.

The applicant is further respectfully directed to Pure and Applied Chemistry, vol 71, No. 4, page 653, which states that ethyl iodide, propyl iodide, and butyl iodide have dipole moments (μ) between 1.8 and 2.1 respectively.

The examiner has interpreted from the references above that Amirav (367) discloses the use of polar molecules in carrier gases for producing positive and negative ions, as recited in claim 22.

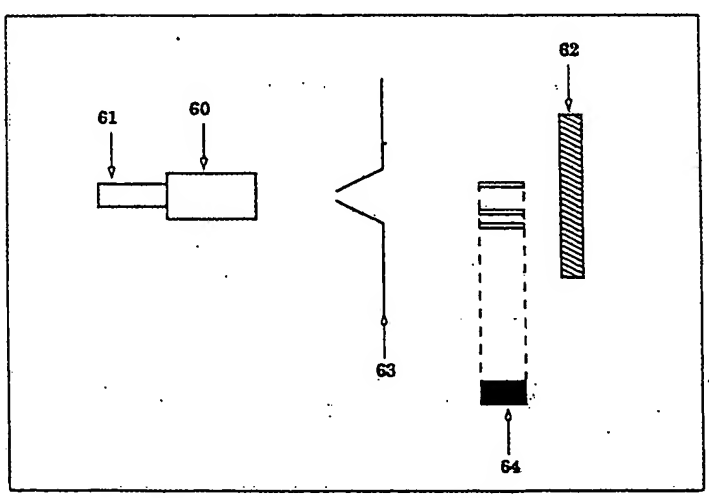
Regarding disclosure of the <u>formation and loading of neutral clusters</u> in Amirav (367);

The applicant is respectfully directed to applicants specification pages 22 and 23, which state; Fig. 6 (below) shows an embodiment of a device according to the present invention for investigating and/or modifying boundary surfaces in the form of a cluster beam system. The cluster beam system is located in a multipart reaction chamber (not shown), which is, for example, constructed like a typical two-chamber molecular beam apparatus (background pressure without cluster beam 10^{-6} mbar....

10^{-7}mbar). The cluster beam system includes a cluster production device 60, 61, possibly with a beam limiter 63, a cluster fragmentation device 62, and a measurement device 64. Furthermore, control and steering devices for the ionized cluster fragments could also be provided, which, however, are known per se as manipulators for charged particles and therefore are not shown separately. The cluster production device includes a nozzle 60 and a supply system 61. The nozzle is preferably a pulsed nozzle with parameters selected depending on the application, but may also be operated continuously.

The operating gas is expanded with a specific expansion ratio (e.g. 1:30), selected depending on the application, at nozzle 60. In the part of the reaction chamber downstream from nozzle 60, a pressure of approximately 10^{-3} mbar obtains. After the expansion, the cluster formation occurs by condensation in a way known per se.

Figur 6



The applicant is also respectfully directed to Amirav (367), Column 4, line 63-68; and Column 5, line 1-3, which states; FIG. 2 contains several other details such as mass 57 of butyl positive ions which is believed to be due to 0.5 percent butyl iodide impurity in the sample which has a higher positive ion yield. A trace amount (0.2 percent) of parent ion peak (M=170) and $(propyl)_2I^+$ (m=213) ions, which we believe are due to clusters of propyl iodide molecules, was also observed (non-linear pressure dependence). Trace amount of I_2 (m=254) ions were also observed.

The applicant is further respectfully directed to Friedman (344), Column 1, line 48-63, which states; Prior to the present invention, neutral clusters were formed by the expansion of gases, usually at room temperature, through supersonic nozzles with the generation of cluster ions through subsequent electron impact ionization. Typically, the gases would flow through a small nozzle from a pressure of about 1 atmosphere to a pressure of about 10^{-3} atmosphere. As the gas expanded and cooled small neutral clusters would form. These clusters would be aerodynamically accelerated to speeds greater than sound, hence the term "supersonic". These clusters would then pass through a further series of nozzles, typically referred to as "skimmers" and "collimators" into regions of still lower pressure, ultimately forming a beam of clusters which would then be charged by electron impact ionization, forming cluster ions by secondary emission of electrons.

The examiner has interpreted from a comparison of the applicant's disclosure and the Amirav (367) references above, that both the applicant and Amirav (367) use equivalent apparati to form neutral clusters via expansion of a carrier gas through a

nozzle and both subsequently ionize the neutral clusters to form cluster ions after impact with a target material, as known in the prior art per the Friedman (344) reference.

Regarding the <u>disclosure of cluster fragmentation in Amirav (367)</u>;

The applicant is respectfully directed to Amirav (367), Column 1, line 39-58, which states; The novel method is based on the discovery that stable molecules undergo molecular ionization and dissociative ionization induced by a collision with a surface at hyperthermal energies. The term "hyperthermal energy range" means larger than the "thermal range", that is, larger than the product of "k" (Boltzmann constant) and "T" (degrees in Kelvin) of the molecular sample, or its container, normally used to define this "thermal energy".

The solid surface impinged by the beam should be one capable of giving or taking an electron from the surface (molecular ionization), or capable of inducing fragmentation into pairs of negative and positive ions (molecular disassociation). The solid surface should also be one, which is chemically inert with respect to the molecules of the beam, and one, which does no tend to neutralize the produced ions, so that the ions that are formed will leave the surface as ions and will not be absorbed. A preferred example of such a solid surface, as described below is clean diamond.

The examiner has interpreted from the Amirav (367) references above, that fragmentation of neutral clusters is disclosed in Amirav (367).

Finally, the examiner has interpreted from all of the above references, as well as the rejection above, particularly as it relates to the discussion regarding Fig. 2 above

that, Amirav (367) discloses the production of neutral propyl iodide clusters by expansion of a propyl iodide seeded carrier gas (the loaded reaction partner) through a nozzle, and subsequently fragmenting some of the neutral propyl iodide clusters into pairs of negative (M=127) and positive ions (M=43), while some of the parent neutral clusters, became ionized clusters (M=170) and (M=213), which were not fragmented. Thus, Amirav (367) and Friedman (344) disclose each and every element of claim 22.

Conclusion

6. The Amendment filed on 9-13-2005 under 37 CFR 1.131 has been considered but is ineffective to overcome the Amirav (367) and Friedman (344) references.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications should be

directed to Phillip Johnston whose telephone number is (571) 272-2475. The examiner can normally be reached on Monday-Friday from 6:30 am to 3:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiners supervisor John Lee can be reached at (571) 272-2477. The fax phone number for the organization where the application or proceeding is assigned is 571 273 8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

PJ
November 18, 2005

JOHN R. LEE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 2800